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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,867	12/28/2000	Steven Alan Dunham	5934-01-EMA	5272

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/719,867	DUNHAM ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6,8-14 and 16-37* is/are pending in the application.

4a) Of the above claim(s) *3 and 25-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,8-14,16-24,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 December 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: copy of Notice re: Power of Attorney.

FINAL ACTION

1. This action is responsive to the Amendment and Remarks filed June 13, 2006, and the complying complete set of claims filed September 25, 2006. Claims 3 and 25-35 remain withdrawn from consideration; applicants' amendment of withdrawn claim 25 is noted. Claim 1 has been cancelled, claims 4-6, 8-9, and 16-21 have been amended, and claim 37 has been added. Claims 4-6, 8-14, 16-24, and 36-37 are now under consideration. Applicants' amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by applicants' amendments. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Undelivered Notice regard Power of Attorney

3. It is noted that a Notice regarding Power of Attorney mailed June 30, 2006 appears to have been returned as undeliverable; however, a Notice of Non-Compliant Amendment mailed August 28, 2006 to the same address was clearly received, as evidenced by the response thereto filed on September 25, 2006. Accordingly, a copy of the Notice of June 30, 2006 is enclosed herewith.

Claim Objections

4. Claims 4, 8, and 16-21 are objected to because of the following informalities: because the claims have been amended so as to depend from new claim 37, the claims

do not depend from a preceding claim but from a subsequent claim (see MPEP 608.01(n)). Accordingly, the format of the claims should be corrected.

Claim Rejections - 35 USC § 112

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS' AMENDMENTS:

5. Claims 4-6, 8-14, 16-24, 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5, 6, 9-14, 22-24 and 36 are indefinite over the recitation "the mutation" in the last line of claims 5 and 6. There is insufficient antecedent basis for this limitation in the claims. It is noted that the preambles of claims 5-6 have been amended to refer to "one or more mutations;" the claims do not refer to a single, particular mutation.

Claim 36 is indefinite because it depends from a claim (claim 1) that has been canceled. The claim refers back to the method of a claim that no longer exists. Accordingly, the claim is incomplete, and the metes and bounds of claim 36 cannot be ascertained.

Claims 37 and dependent claims 4, 8, and 16-21 are indefinite because it is unclear how steps b)-c) and e)-f) of claim 37 relate to one another and to the method of the claims. Particularly, each of steps b) and e) require isolating PCR products; however, subsequent steps c) and f) (respectively) refer back to products of steps a) and d) (respectively). Thus, it is unclear as to how or whether the isolated products of steps b) and e) are employed in the claimed method.

Claims 37, 4, 8, and 16-21 over the recitation of the limitation "a wild type strain" in steps h) and j) of claim 37. It is noted that prior steps d) and f) refer to "the wild type strain," making clear that these steps employ the same strain recited in step a). It is not clear whether the recitation of "a wild type strain" in steps h) and j) also refers to the wild-type strain of a), or whether the claims might encompass the use of another bacterial strain. To the extent that the claims might encompass the latter, the claim does not make clear how one could identify mutations conferring resistance using a different wild-type strain. Clarification is required.

Claim 4 is indefinite because it is not clear how or whether the claim further limits claim 37, from which it depends. The claim is drawn to the "use of the process according to claim 37 for identifying and characterizing drug-target interactions." While the claim clearly requires the process of claim 37, the language of the claim gives no indication as to how one is to accomplish the identifying and characterizing recited in claim 4. The claim should be amended so as to provide active, positive steps that indicate how this use is actually practiced (see MPEP 2173.05(q)).

Claim Rejections - 35 USC § 103

6. Claims 5-6, 9, 22, 24, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kok et al. (Journal of Bacteriology 179(13):4270-4276 [7/1997]) in view of Minshull et al. (US Patent No. 5,837,458 [11/1998; filed 5/1996]), for the reasons set forth in the Office action of February 13, 2006.

The response traverses the rejection on the following grounds.

First, the response notes that the Kok et al reference "does not teach or suggest that it would be desirable or possible to randomly mutagenize the entire chromosome of a bacterium," and that Kok et al do not "teach or suggest the use of PCR products of approximately 10 kb to approximately 15kb." This argument is not persuasive. The absence of these teachings in the Kok et al reference was acknowledged in the Office action of February 13, 2006, with the Minshull et al reference clearly being cited for its suggestion of these claim limitations that were absent in Kok et al. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Next, the response argues that "Minshull et al. does not suggest providing random mutagenesis to encompass the complete chromosome or to use overlapping PCR products of approximately 10 kb to 15 kb," and that "Minshull et al. do not specifically identify any mutations that confer resistance to a compound, nor do they identify the site of any mutation generated," noting that "Minshull et al. are concerned with recursive sequence recombination." These arguments are not persuasive because applicant is again attacking a reference (Minshull et al) individually while the rejection is based on a combination of references; the teachings of random mutagenesis and mutation identification are present in the Kok et al reference, as was clearly stated in the rejection of February 13, 2006. Further, Minshull et al do teach methods comprising PCR mutagenesis, teach the analysis of entire genomes, and teach the generation of a wide range of variant fragments encompassing the range of 10 kb to 15 kb (see the

rejection of February 13, 2006). With further regard to the size range claimed, it is noted that a range that lies within a range disclosed in the prior art is *prima facie* obvious (see discussion in MPEP 2144.05). It is also noted that Applicants have not provided, e.g., any evidence of unexpected results obtained with this particular range.

The response further argues that there would not have been a reasonable expectation of success that the method of Kok et al in view of Minshull et al would work, and particularly, "that one could search the entire chromosome using PCR and identify one or more mutations conferring resistance to a compound." This argument has been thoroughly considered but is not persuasive. While one of ordinary skill in the art would clearly have expected the claimed method to be labor intensive, techniques of PCR, PCR mutagenesis, and mutation identification were routine in the art at the time the invention was made. Thus, while there would be an expectation that the examination of a complete chromosome would require more time and reagents than examination of, e.g., a gene or operon, an ordinary artisan would clearly have expected that these routine methods could be employed successfully in analyzing a complete chromosome. Regarding applicants' arguments that it would not have been obvious to "pool groups of these 10 kb to 15 kb products that correspond to 100 kb of the chromosome," etc., it is noted that the instant claims do not recite such limitations. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The references of Kok et al and Minshull et al suggest all the limitations of present claims 5-6, 9, 22, 24, and 36, and therefore this rejection is maintained.

7. Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kok et al. in view of Minshull et al. as applied to claims 5-6, 9, 22, 24, and 36, above, and further in view of Belland et al. (Molecular Microbiology 14(2):371-382 [1994]), for the reasons set forth in the Office action of February 13, 2006.

First, the response traverses the rejection for the reasons set forth in paragraph 6 with regard to the Kok et al and Minshull et al references. The response to those arguments set forth in paragraph 6 applies equally herein. With regard to the instant rejection, it is noted that the Belland et al reference was cited merely for its teaching of an antibiotic not specifically recited in the Minshull et al reference, and its teaching that one may screen for mutations that confer resistance to that antibiotic (the fluoroquinolone ciprofloxacin). The reference was not cited for any teachings with regard to PCR mutagenesis or amplification, mutation characterization techniques, analysis of complete chromosomes, etc., as discussed in applicant's response. Accordingly, applicants' arguments with regard to these features not being taught in Belland et al are not persuasive. With regard to a reasonable expectation of success, it is noted that applicants' arguments pertinent to this issue are addressed in the preceding paragraph.

The references of Kok et al, Minshull et al, and Belland et al suggest all the limitations of present claims 10-11, and therefore this rejection is maintained.

8. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kok et al. in view of Minshull et al. as applied to claims 5-6, 9, 22, 24, and 36, above, and

further in view of Pruna (U.S. Patent No. 5,532,239 [7/1996]), for the reasons set forth in the Office action of February 13, 2006.

First, the response traverses the rejection on the grounds that Kok et al and Minshull et al do not teach the method of the claim. The response to those arguments set forth in paragraph 6 applies equally herein. It is noted that the Pruna reference was cited merely for its teaching of an antibiotic not specifically recited in the Minshull et al reference (clinafloxacin); the reference was not citing for any teaching of PCR mutagenesis, PCR products, etc., as discussed in applicants' traversal. Accordingly, applicants' arguments with regard to these features not being taught in Pruna are not persuasive.

The references of Kok et al, Minshull et al, and Pruna suggest all the limitations of present claim 12, and therefore this rejection is maintained.

9. Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kok et al. in view of Minshull et al. as applied to claims 5-6, 9, 22, 24, and 36, above, and further in view of Ibrahim et al (U.S. Patent No. 5,145,667 [9/1992]), for the reasons set forth in the Office action of February 13, 2006.

The response traverses the rejection on the grounds that the Ibrahim et al reference does not disclose methods of mutagenesis, mutation identification, PCR of a complete chromosome, etc. However, it is again noted that these features are taught or suggested by the combined references of Kok et al and Minshull et al. The Ibrahim et al reference was cited merely for its teaching of an antibiotic not specifically recited in the Minshull et al reference. Accordingly, applicants' arguments are not persuasive.

The references of Kok et al, Minshull et al, and Ibrahim et al suggest all the limitations of present claims 13-14, and therefore this rejection is maintained.

10. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kok et al. in view of Minshull et al. as applied to claims 5-6, 9, 22, 24, and 36, above, and further in view of Wohlstader (U.S. Patent No. 6,087,177 [7/11/2000; filed 3/16/1992]), for the reasons set forth in the Office action of February 13, 2006.

The response traverse the rejection on the grounds that the Wohlstader references fails to overcome "the deficiencies of Kok et al. in combination with Minshull" with regard to PCR mutagenesis of complete chromosomes, PCR product size, etc. The response to these arguments regarding Kok et al and Minshull set forth in paragraph 6 apply equally herein. The Wohlstader reference was cited merely for its teaching of UV irradiation. Accordingly, applicants' arguments regarding the absence of other teachings in the Wohlstader reference are not persuasive.

The references of Kok et al, Minshull et al, and Wohlstader suggest all the limitations of present claim 23, and therefore this rejection is maintained.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
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Art Unit 1634